The Other White Meat.

National Pork Board

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 98D-1146

"Draft Guidance for Industry: Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern" (Guidance #152).

Dear Sir or Madam:

These comments are submitted on behalf of the National Pork Board in response to your request for comments. The National Pork Board was established by an act of Congress in 1985 and is responsible for the collection, distribution, and program accountability for the money generated by the pork checkoff. A Board led by 15 pork producers creates programs in the areas of promotion, research, and consumer information. These programs support producers by providing them with information on many areas including swine health and pork safety. The information contained in this communication is intended to share scientific information and experiences generated by producer checkoff investments and the application of that information to pork production.

Food safety and animal health are priorities of the nation's pork producers and the National Pork Board shares the concern for the impacts that antimicrobial use on the farm has on these issues. The National Pork Board has adopted the following position statement on the use of antimicrobials in pork production:

> "It is essential to public health and food safety, animal health and well-being, and the environment to maintain the effectiveness and availability of antimicrobials. All decisions affecting the availability of antimicrobials for animal use need to be transparent and based on sound science. The National Pork Board supports the use of antimicrobials only when they provide demonstrable benefits and urges producers to:
>
> - take appropriate steps to decrease the need for their application;
> - adhere to judicious use guidelines;

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pork checkoff

- assess the benefits and costs of all uses of antimicrobials; and
- complete the Pork Quality Assurance Program and fully implement into their daily operations the management practices described for responsible use of animal health products."

In 1998, in their "American Veterinary Medical Association Judicious Use of Therapeutic Antimicrobials" document, the AVMA adopted the definition of therapeutic uses of antimicrobials as including the "treatment, control, and prevention of bacterial disease." Subsequently the American Association of Swine Veterinarians provided its members clarification of the AVMA Judicious Use Principles in its "American Association of Swine Veterinarians Basic Guidelines of Judicious Therapeutic Use of Antimicrobials In Pork Production." These guidelines include consideration of the herd health history for the therapeutic use of antimicrobials in the control and prevention of disease and the AASV instructs its members that when these factors are appropriately considered, preventative therapy is a judicious use of antimicrobials.

Then, FDA-CVM published in August of 2001the booklet, "Judicious Use of Antimicrobials for Pork Producers." In it FDA-CVM defines therapeutic use as "treatment, control and prevention of bacterial disease" and instructs pork producers that judicious use includes to "limit therapeutic antimicrobial treatment to ill or at-risk animals, treating the fewest animals indicated." As explanation, FDA-CVM continues, "Decisions to administer individual or herd therapy should be based on experience, farm history and the prevalence or risk of disease in the group. Judicious use of therapeutic antimicrobials includes using these drugs only when necessary to treat, prevent or control disease. There may be times when using antimicrobials to prevent disease will mean ultimately less antimicrobials will need to be used." (underlining added for emphasis)

As the National Pork Board position statement reads, we strive to adhere to judicious use guidelines on our farms. It is essential that producers have a variety of cost-effective antimicrobials available in a timely manner for these therapeutic purposes as defined by the AVMA, the AASV and the Agency.

We would like to thank the Agency for its work in trying to provide an orderly way to evaluate public health risk from agricultural uses of antimicrobials. However, we have serious concerns about the implementation of Guidance #152. If the Guideline would be fully implemented as written, the bar of acceptance for an antimicrobial to be used in herds of food producing animals could be so high that it could be unattainable and could affect timely, cost-effective availability of antimicrobials for animals. This is important to us because it could cause unintended consequences that compromise the health and welfare of our animals, the safety of our food supply, and the quality of our environment.

Following are comments organized according to the applicable section of the Guidance document:

III. Risk Analysis Methodology; C. Data sources/data quality:

There is a lack of a decision-making process that is based on a peer-reviewed body of scientific evidence and transparency. The Guidance asks for sponsoring companies to use either published literature or prospective studies to supply data supporting their

submitted risk analysis of their product. However, 33% of the Guidance relies on the ranking of antimicrobials according to their importance in human medicine, which does not include any data to support the ranking. In the first instance, CVM is saying that a risk analysis should be based on data and in the second instance it does not provide the data that it, itself, has used to set the importance of the individual antimicrobials to human health. Is this data available for review?

V. Qualitative Antimicrobial Resistance Risk Assessment; A. Release Assessment:

In pork production, it is unrealistic to expect that therapy for a disease – treatment, prevention or control – can always be accomplished by individual dosing. The Guidance penalizes an antimicrobial for use in a herd without giving specific information about an "acceptable" size of the population. Applying this criterion of the extent of use of the proposed product (individual vs. small groups vs. flocks/herds) necessitates defining each of these terms and then justifying how, based on scientific evidence, the size of the group is a determining factor in the emergence of antimicrobial resistance. How big is a small group? Over 5 animals? 10? 100? 1000? This criterion appears in both the Release Assessment and in the Risk Management Consideration, which gives it added weight in the decision-making process.

Defining a herd or population of pigs is dependent on the type of operation. Although there is a very wide range of types of production and herd sizes, market pigs are typically housed in pens of 25 to 30 pigs in barns containing around 1,000 animals. The number of barns on a site is dependent on the production system. Four barns per site is not unusual. The number of barns or the number of animals in the barn may be smaller for producers with smaller herds. Therefore, one barn may represent up to 100% of the operation's pigs.

Because pigs in a group typically have common age, immune status, housing environment, etc., when a disease is introduced into the population or is endemic all the animals are either affected or at risk from the disease. Responding to the disease with therapeutic medication for disease treatment, prevention, or control is usually necessary for the whole herd (where all the animals are in one group or barn) or a percentage of the herd (where the barn is one entity containing a defined number of the pigs on the site). **In either case, it is possible to define the pigs in the barn as a discrete population of pigs to which the delivery of medication by the feed or by the water is possible and controllable. The needs of the animals would be met if the definition of the term "select groups" (Table 4) included discrete populations such as those housed in a barn.**

It is not always feasible to isolate and individually treat all ill pigs. They must be treated in the pen in which they reside because the cohorts in each pen have formed a social hierarchy. Removing a pig, even for a limited period of time, may upset that hierarchy sufficiently that reintroducing the pig could result in fighting and aggression, even to the point of the group killing the reintroduced pig.

Depending on the disease and the conditions of the pigs, individual treatment in pens may be attempted. But, when the incidence of the disease in the barn exceeds usually around 10% of the animals, the water and/or feed is necessary to deliver the required medication. With large groups of animals, it is not realistic to inject all the animals on the multiple days

that medication may need to be delivered. Multiple individual injections may compromise animal welfare, meat quality and human safety. It is more appropriate to use water or feed medication delivery methods in order to prevent further illness and animal suffering and to use antimicrobials efficiently and judiciously.

This criterion attempts to set some limiting size parameters around the group of animals to be treated. In practice on the farm, the ability to rapidly provide medication to all the animals that are either ill or at risk is the primary consideration. **The focus should be on the group of animals to which medication delivery can be controlled and not simply the number of animals in the group.** In some operations, the appropriate group might be the pigs in a pen. In others, the pigs in the entire barn are the group that is appropriate to medicate and to which medication delivery is controllable.

In some disease outbreak situations, it is necessary to deliver medication for a period of time longer than just that necessary to treat the initial outbreak. Disease treatment in populations may not eliminate the pathogenic agent. For example, in outbreaks of diseases like Swine Dysentery or enteric Salmonellosis, it may be necessary to continue medication delivery to the population at a defined dose for a prescribed period of time in order to continue to control the disease outbreak. Otherwise the disease will continue to reoccur, resulting ultimately in more medication being used, increased pain, suffering and mortality within the group, and possibly an increased risk of bacterial resistance through the periodic exposure to the antimicrobial.

V. Qualitative Antimicrobial Resistance Risk Assessment; B. Exposure Assessment:

The Guidance overestimates the risk to people from eating pork because it doesn't speciate zoonotic bacteria and thus doesn't account for commodity differences in the prevalence of species. It also uses out-of-date FSIS HACCP baseline data to estimate bacterial prevalence in food.

Campylobacter jejuni causes over 90% of the human cases of campylobacteriosis, but *C. jejuni* is rarely found in pigs in the United States. *Campylobacter coli* is the predominant serotype found in pigs and yet is isolated in only 3-4% of human cases of campylobacteriosis. In recent CDC FoodNet case-control studies, consuming pork was not identified as a significant risk factor for infection. In addition, 50% of the *C. coli* isolated from studied human cases of diarrhea is resistant to fluoroquinolone, indicating that it was derived from a non-pork source. (Personal Communication, Dr. Fred Angulo, Centers for Disease Prevention and Control, Atlanta, GA, November 14, 2002) Assigning an exposure assessment based only on the prevalence of the *Campylobacter* genus unfairly penalizes the availability of antimicrobials to pork producers.

The data collected in 1995 to 1996 that is used in the Guidance to estimate bacterial prevalence in food is out-of-date. The prevalence of *Salmonella* contamination on pork carcasses has decreased by approximately 50% since this baseline study and it is reasonable to assume that the same interventions that have caused the decline in *Salmonella* have also been effective in reducing *Campylobacter* contamination. Without current survey data, including speciation, it would seem inappropriate to consider pork as a high risk for human campylobacteriosis.

The Guidance doesn't acknowledge that the majority of consumed pork is further processed in ways that can decrease the likelihood of bacterial contamination. An estimated 65% of consumed pork products are further processed from raw meat in ways that may decrease

the prevalence or inhibit the growth of bacteria. The way the Guidance is now written, even irradiation to the level that the meat would be rendered sterile would not result in a low risk category for many antimicrobials. Setting the qualitative risk level as suggested biases the results to the highest levels of risk and would likely result in limitations on the availability of antimicrobials to pork producers.

V. Qualitative Antimicrobial Resistance Risk Assessment; C. Consequence Assessment:

Because the body of scientific evidence used to rank antimicrobials according to their importance in human medicine is not presented, that ranking can be viewed as arbitrary and subjective. Use of antimicrobials in food producing animals is being implicated in resistance of bacteria that cause tuberculosis, Legionnaires Disease, and venereal infections. There is no data provided to support the contention that foodborne bacteria can contribute to resistance in these diseases. Since 33% of the final categorization of risk is dependent on this ranking, essentially all antimicrobials important to swine medicine are *a priori* assigned to Category 1 or 2 and thus their availability is severely limited. Without supporting data, this section of the Guidance document is akin to the European Precautionary Principle and more emotional than scientific.

There is no scientifically based quantification of the actual risk of the *in vivo* transfer of resistance determinants among commensals and zoonotic pathogenic bacteria. Although *in vitro* transfer of some of these elements has been demonstrated, specific laboratory conditions have been necessary. Describing resistance determinant transfer in the animal as a credible, quantifiable risk to public health requires many steps that must fall into a specific sequence and at a level sufficient to cause public health consequences. Applying to the regulation of animal health products the theory that all the factors can successfully come to pass in the animal is using the Precautionary Principle to prevent the availability of antimicrobials to agriculture.

VI. Antimicrobial Resistance Risk Management Consideration:

It is imperative to animal health, food safety, animal welfare and the environment that food animal producers maintain the cost-effective and timely availability of antimicrobials to respond to their animals' needs. Proposed risk management steps would likely severely limit this availability.

The examples of risk management steps include prescription or Veterinary Feed Directive for Categories 1 and 2, categories in which the great majority of antimicrobials will fall. In some areas of the country, this will affect the timely availability of antimicrobials and the ability to quickly respond to animal disease because there aren't enough veterinarians with swine expertise to meet the needs of producers. In addition, this will put an extraordinary financial and record-keeping burden on producers without any evidence that there will be any effect on antimicrobial resistance or any benefit to public health.

The Guidance also provides for FDA-CVM to prohibit the extra-label use of antimicrobials (use as directed by a veterinarian in a dosage, route of administration, indication, or species other than what is written on the label). While this could be an important tool to protect public health in specific instances, it is possible that the Guidance could be used for broad, sweeping extra-label

use prohibitions. If that happens, it could have serious consequences on animal health, welfare and production. We do not now have an adequate arsenal of antimicrobials to address the health needs of our animals with labeled products. It is often through extra-label use directed by the veterinarian using his or her professional judgement and knowledge that we are able to maintain our animals' health and the safety of the food supply. To prohibit critically needed extra-label use without significant supportive scientific evidence would not seem appropriate.

In conclusion, the nation's pork producers would like to offer their assistance in providing technical advice about the realities of today's modern pork production practices as the Agency considers revisions to the Guidance document.

Sincerely,

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